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ACUTE PANCREATITIS—PARAPANCREATIC ABSCESS—DISSEMINATED FAT-NECROSIS.[1]

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W. D., aged thirty-four years, married, piano-polisher.

Family history. Father died of "old age," at seventy-eight years; mother died of "dropsy;" six brothers and four sisters living; one brother died at the age of thirty-seven of apoplexy; no history of tuberculosis in any branch of family.

Personal history. As a child had chicken-pox; pneumonia at the age of six years; has been married thirteen years; has had no children. For years he has been a regular drinker of beer and whiskey; he usually takes a drink of whiskey in the morning before breakfast; sometimes more in the day; smokes and chews tobacco. Five years ago the patient states that he was overcome by heat. He was in bed a week, and unconscious at times during that period. Ever since this attack he has had, at times, peculiar "scary spells," a nervous dread of some impending disaster. For about two years he has been subject to nausea in the morning; at times he vomits a greenish, slimy substance. Frequently he vomits his breakfast on account of this feeling of nausea. For the last year and a half the patient has had several attacks of very severe cramp-like pain in the abdomen. The pains are localized in the median line, across the epigastrium and about the umbilicus. The first attack came on at night, and was very severe. The pains are relieved only by morphine, which has been administered in large doses. After the sleep following the relief given by morphine, the patient is free from pain, but with each attack he has generally remained away from work and in the house for from several days to a week. He thinks he has had fever with these attacks, which are also often associated with vomiting. He has had, in all, three or four paroxysms of this nature. The attacks have never been associated with jaundice.

On Friday, the 15th of June, 1895, the patient came home from work on account of a slight sensation of heaviness in the epigastrium and an anxious feeling which he had noticed before to precede the attacks of pain. On Friday night the pain became very severe, and was associated with vomiting. The pain was intense and continuous, and a swelling was noticed just above the umbilicus, in the area of greatest tenderness. There was constipation. During the next week the patient was in bed; at times he was delirious; there was continuous fever; a diagnosis of abscess of the liver was made by his physician.

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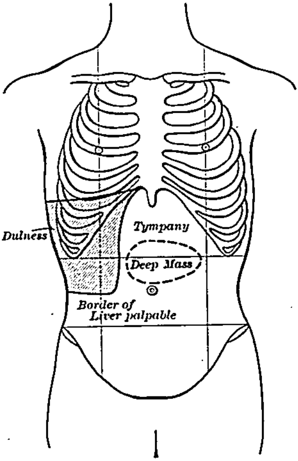
[1] Read before the Johns Hopkins Hospital Medical Society, Jan. 7, 1895.

On June 25th the patient was admitted to the Johns Hopkins Hospital, operation having been advised. He was admitted to the surgical department of Professor Halsted, Dr. J. M. T. Finney in charge. To the courtesy of Professor Halsted and Dr. Finney I owe the opportunity of examining and following this case.

I saw the patient shortly after his entry, and made the following note: "On physical examination the patient is a well-formed man, quite corpulent; lips and mucous membranes of good color. The tongue is coated, the temperature elevated; the mental condition dull; the patient is a little confused. Examination of the *thorax* is negative. On inspection the *abdomen* is full, showing a rather undue prominence in the median line across the epigastrium. Hepatic flatness begins at the sixth rib in the mammillary line, while in the same line the lower border of the liver can, apparently, be felt about on a level with the umbilicus; it is not, however, very distinct, owing to the tension of the abdominal muscles. Liver-flatness is coextensive with this area. Passing toward the median line the resonance becomes tympanitic. Just below the xiphoid cartilage the resonance is loudly tympanitic, and from the sensation conveyed by palpation there is evidently an air-containing organ (stomach?) just below the skin. Below, between this and the umbilicus, at the point of maximum prominence, is to be felt a deeply-seated mass, over which there is well-marked tympany. The outline of the mass



is indistinct. It is not tender on ordinary palpation. To the right this mass is not to be sharply separated from what would appear to be the liver; to the left it reaches about to the costal region. Pressure over the lower left ribs does not cause pain. In the knee-elbow position nothing further is to be made out. *Splenic* dulness is about normal in area, and does not pass the costo-articular line. There are no glandular enlargements." The appended chart, made at the time of this examination, shows the position of the deep mass, of the hepatic dulness, and the epigastric tympany.

The *urine* was free from albumin or sugar.

The *blood* showed a leucocytosis.

From the fever and general condition of the patient it was believed that there was an acute intraperitoneal inflammatory process. Though the mass was not distinctly fluctuating, it gave, on palpation, the impression that it contained fluid, and the diagnosis lay between an hepatic abscess, an abscess resulting from perforation of the stomach or intestine, and an acute inflammatory process, starting, probably, from the pancreas. While no sharp separation could be made out between the deep mass and the liver, the absence of motion on deep inspiration, the sharp outline of the hepatic dulness, the loss of the lower border of the liver, which was to be made out on palpation to the right of the mass, as well as the entire absence of jaundice, made the presence of an hepatic abscess improbable. A fecal abscess was not to be definitely ruled out, though the situation was certainly unusual. There was nothing in the history of the case to suggest the existence of a perforating gastric or duodenal ulcer. Nothing pointed to implication of the gall-bladder. On the other hand, the situation of the mass, which was deep, was exactly that of the pancreas. The history of the case was, also, not unlike that in other cases of acute pancreatitis which have been reported. The patient was a fat man, with a somewhat alcoholic history. There had been several sharp attacks of pain, localized quite definitely in the pancreatic area, associated with fever, vomiting, and collapse. That the mass might be a pancreatic cyst, or a cyst of the lesser omentum, appeared improbable, owing to the suddenness of the appearance of the tumor, to the inflammatory nature of which the fever and general symptoms strongly pointed.

The diagnosis, then, of acute pancreatitis with disseminated fat-necrosis, and possible sequestration of the pancreas, was made, and an exploratory operation advised.

The operation was performed under ether, on June 27th, by Dr. Finney. An incision was made in the median line above the umbilicus. On opening the peritoneal cavity the large right lobe of the liver was found on the right, much as indicated by the dulness upon the chart. In the median line, adjoining the liver and stomach, a mass of adherent fatty tissue was found, which was filled with numerous discrete and confluent small, opaque, yellowish-white nodules, presenting the characteristic appearance of disseminated fat-necrosis. This mass of tissue was adherent to the stomach and to the liver. Involved in the adhesions over the lower part of the opening passed the transverse colon. The general abdominal cavity was packed off with gauze, and an opening was left for future drainage.

For the next several days the temperature remained somewhat elevated, but the general condition of the patient was fairly good.

On July 3d, on dressing the wound, the tumor-mass was found to have diminished considerably in size.

On the 5th and 6th of July the patient was restless, nauseated, and, at times, delirious. On the evening of the latter date a small coil of intestine was expelled, on coughing, from the lower end of the wound; it was returned without subsequent trouble.

At 10 P.M. on the 7th an examination was made by Dr. Halsted. The examining finger opened, in the upper angle of the wound, a large cavity containing thick, brownish-yellow pus and large masses and shreds of necrotic fat. The finger passed far backward at the bottom of the wound into what appeared to be a cavity in the pancreas. The main excavation represented, evidently, the lesser peritoneal cavity. A drainage-tube was placed in the wound, which continued to discharge. Several days later the wound presented an interesting appearance. Across the middle of the incision stretched the transverse colon, which presented a raw and granulating surface, while above this an opening extended into the large cavity, discharging creamy pus and large masses of necrotic fatty tissue. The cavity was drained freely, and slowly granulated and contracted, while the general condition of the patient improved greatly.

The patient left the hospital on the 23d of September, feeling quite well. The wound at this time was entirely closed excepting for a small sinus, which was two inches deep and one and a half inches in diameter.

The discharge from the cavity on the day after the opening was made showed pus-corpuscles, bacteria in great quantities, numerous fatty acid crystals, with large and small masses of necrotic fat. Cultures were, unfortunately, not made, the opening occurring unexpectedly. No tissue which could be identified as pancreatic was found in the discharge. Some of the detritus discharged from the wound was placed in alcohol and hardened, while sections were examined under the microscope. These masses proved to consist simply of necrotic fatty tissue. Several small pieces of the fat found at the first operation were removed and sent to the pathological laboratory, to Dr. Barker, who made the following report: "The naked eye shows here and there in the tissue opaque white areas which are entirely different in appearance from the rest of the fat. They remind one of particles of tallow; they are slightly grayish and inclined to be granular. Under a low power one observes masses which tend toward a spherical shape, though they are often irregular in outline, with a peculiar yellowish tint. Some of the masses appear more or less homogeneous, showing fissures, transverse or radiating from the centre, not unlike the appearance of hyaline muscle in infectious diseases. Other masses of similar size are seen under the high-power to consist of myriads of short acicular crystals arranged usually more or less irregularly, sometimes radially placed. There are many single crystals and bundles of crystals, resulting evidently from the breaking up of these masses. Some of the large, apparently homogeneous bodies show within them what appear to be large radiating crystals, resembling the so-called margarine crystals. In addition to these there are numerous small masses, the substance of which, in its homogeneous appearance, resembles much that of the larger homogeneous bodies.

"On application of heat, after mixing the mass with salt-solution, the homogeneous bodies become flatter, sometimes fuse, and show still more the appearance of hyaline muscle.

"On heating the tissue with cold glacial acetic acid the crystals and masses are rapidly transformed into fat-droplets. Each single crystal can be watched changing into a fat-droplet. Many of them which meet one another fuse. There is a marked activity in the masses with an almost immediate transformation of the substance into minute fat-droplets. These remain separate for a while, but later fuse, especially if the cover-glass be pressed. There is a rapid appearance of fat-drops at the edge, with violent streaming movements. Toward the centre the action is very slow and the acicular crystals become at first much more distinct. Both the crystals and the homogeneous substance dissolve.

"On treating with hot glacial acetic acid there is a rapid transformation into fat-globules. In sections the same process takes place, large, clear spaces of fat being seen in the transparent tissue.

"The masses do not dissolve in absolute alcohol nor in ether.

"20 per cent. hydrochloric acid in 70 per cent. alcohol acts as does cold glacial acetic acid, though rather more rapidly. Pure hydrochloric acid produces, also, the same changes.

"10 per cent. caustic potash, hot or cold, produces no marked change.

"Oxalic acid alone has no special influence, but, after treating the nodules of fat-necrosis with glacial acetic acid, the subsequent addition of oxalic acid gives an immediate white precipitate, while later typical crystals of calcic oxalate may be made out microscopically."

These observations confirm entirely the views of Langerhans,[1] who demonstrated that these fat-necroses consisted of a combination of lime with fatty acids.

Cultures on slant agar from the necrotic areas and from the adjacent tissues were negative. Cultures made at the operating-table from similar areas were also negative.

The operation, then, revealed a deep-seated abscess occupying the lesser peritoneal cavity, arising apparently from the pancreas. This was associated with extensive disseminated fat-necrosis.

Acute inflammatory affections of the pancreas have occupied considerable attention during the last five years, since the appearance of Dr. Fitz's Middleton-Goldsmith Lectures on Acute Pancreatitis.[2] Fitz collected from his own cases and literature fifty-four examples of acute pancreatitis, where satisfactory accounts of the cases were given, as well as sixteen cases of extensive hemorrhage from the region of the pancreas. From careful analysis of these cases he concluded that acute inflammation of the pancreas was a "well-characterized disease," one which could and should be more often recognized. He divided these cases into three main classes: (1) *suppurative pancreatitis*; (2) *hemorrhagic pancreatitis*; and (3) *gangrenous pancreatitis.*

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[1] Verhandl. d. x. Internat. med. Cong., Bd. ii. abth. iii. p. 144, Berlin, 1891, 8vo., and Virchow's Archiv, Bd. 122, p. 252, 1890.

[2] Acute Pancreatitis, Boston, 1889, 8vo. Also Bost. Med. and Surg. Journal, v. xxi. pp. 181, 205, 227, 1889.

(1) In *suppurative pancreatitis* there exists an acute purulent inflammation of a smaller or larger part of the pancreas.

(2) In *hemorrhagic pancreatitis* the process consists of an acute cellular or fibrino-cellular infiltration of the connective tissue of the organ with a more or less extensive necrosis of the lobules. This inflammatory process is associated with numerous diffuse hemorrhages throughout the organ; these may sometimes be quite extensive; these cases are not to be confused with those instances of extensive apoplectiform hemorrhage which are not so uncommon in the pancreatic region.

(3) The *gangrenous pancreatitis* appears in many cases to be an after-result of an attack of acute hemorrhagic pancreatitis. Here the peritoneal covering of the pancreas may be destroyed, while large or small portions of the organ may be sequestrated. Perforation into neighboring organs may occur, and discharge of the necrotic pancreas by the rectum has been noted in two instances.

Disseminated fat-necrosis was noted in nearly half of the cases of hemorrhagic and gangrenous pancreatitis; it was less commonly seen in the suppurative forms.

Clinically the symptoms presented by these cases formed quite a striking picture, consisting usually of[1] "sudden, severe, often intense, epigastric pain, without obvious cause, in most instances followed by nausea, vomiting, sensitiveness, and tympanitic swelling of the epigastrium. There are prostration, often extreme, frequent collapse, low fever, and a feeble pulse. Obstinate constipation for several days is the rule, but diarrhœa sometimes occurs. If the case does not end fatally in the course of a few days, recovery is possible, or a recurrence of the symptoms in a milder form takes place, and the characteristics of subacute peritonitis are developed." The cases of hemorrhagic pancreatitis are usually very acute and often fatal within a few days. When the process is not immediately fatal it may last a little longer, going on possibly to sequestration and gangrene. The cases of suppurative inflammation of the pancreas may, in some instances, last for weeks or months.

The differential diagnosis, according to Fitz, lies "between an irritant poison, perforation of the digestive or biliary tract, and acute intestinal obstruction."

Since the appearance of this paper a considerable number of cases of acute pancreatitis have been reported by Dr. Fitz[2] himself and by other authors. The study of the literature shows that most of the cases would fall under Fitz's headings of hemorrhagic or gangrenous pancreatitis, where this case also probably belongs, the extensive parapancreatic abscess being probably a secondary process. A case which was very similar to that above reported was noted by Walsh.[1] Here a similar abscess was found and successfully drained. The symptoms had been of six months' duration, consisting of "sharp burning pains in the epigastric region and tenderness on pressure." The physical examination showed "an area of dulness extending from the ensiform cartilage half way to the umbilicus and reaching to the left costal area."

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[1] Loc. cit., p. 89.

[2] Trans. Assoc. Amer. Phys., 1890, p. 191, and Bost. Med. and Surg. Journal, vol. cxxvii, p. 573.

The cause of these inflammatory processes is not by any means entirely clear. Fitz[2] believes that they are due in most instances to infectious agents entering through the pancreatic duct. The presence of biliary or pancreatic calculi seems to be somewhat favorable to their development.

One of the most interesting points, however, in connection with these cases of acute pancreatitis is the frequent association of the condition which was first described by Balser[3] as disseminated fat-necrosis. The very common association of fat-necroses with acute pancreatitis naturally suggests that there is some close relation between the two processes, and the views as to the nature of these fat-necroses and as to their association with acute pancreatitis it may not be uninteresting to summarize. Balser believed these areas to be due to an excessive growth of fatty tissue, which destroyed the tissue which it surrounded, the central portions of fat becoming necrotic from lack of nutrition. He found these areas of fat-necrosis in the interlobular fat in a number of bodies where no special symptoms had been present during life. The changes in the pancreas he believed to be secondary.

Chiari[4] was unable to find any evidence of this overgrowth of fatty tissue and regarded the process as degenerative, the result simply a condition of general marasmus.

Fitz[5] is inclined to believe in two varieties of fat-necrosis; first, a simple "necrobiotic" fat-necrosis, which has, he believes, no direct relation to severe pancreatic lesions; and secondly, an inflammatory fat-necrosis, which he believes to be generally secondary to an acute inflammation of the gland. This process may be extensive and lead to sequestration of the organ. The fat-necroses are not the cause of the hemorrhages in hemorrhagic pancreatitis. The hemorrhages result from the infectious process, which is also the cause of the necrosis. The inflammatory nature of these areas, Fitz believes, is suggested by the round-celled infiltration which one always finds about their periphery, and by the fact that microscopically he has, in several cases, demonstrated the presence of bacteria in or about the affected spots.

Langerhans[6] in two interesting communications demonstrated that the substance of these necrotic areas consisted in a combination of certain lime salts with fatty acids. These observations Prof. Welch has been able to confirm in a number of instances. The observations of Dr. Barker in this case were also wholly confirmatory of these views. Later Langerhans[1] makes the interesting suggestion that the process may possibly result from the action of the fat-splitting ferment from the pancreas upon the surrounding fat-tissue, the fatty acids entering afterward into combination with lime. He asserts that in one instance he has been able to produce similar changes in the subcutaneous fat of a dog by the injection of an extract of the pancreas.[2]

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[1] Medical News, Phila., Dec. 1893, p. 737.

[2] Trans. Assoc. American Phys., 1890.

[3] Virch. Archiv, Bd. 90, S. 520, 1882.

[4] Prager med. Woch., 1893, No. 30, S. 285, and No. 31, S. 299.

[5] Acute Pancreatitis, Boston, 1889, 8vo.

[6] Loc. cit.

Rolleston[3] suggests that they are rather due to some trophic influence exerted by the abdominal sympathetic system, which is very probably affected in most of these instances by the extension of some morbid process from the pancreas.

Balser[4] in 1892 made a preliminary communication in which he stated that in certain areas of fat-necrosis in hogs he had found numbers of fine rod-like bodies collected often into aster-like masses. These rods were somewhat thickened at one end, resembling the "clubs" of actinomycosis. From their staining-reactions he believed that they were not crystals but bacteria.

Culture-experiments, though unfinished, showed growths of a short rod-like bacterium. No further communication on the subject has, however, appeared.

Prof. Welch[5] in 1891 obtained the bacillus coli communis in pure culture from areas of fat-necrosis associated with acute hemorrhagic pancreatitis. There was, however, a general colon infection following extensive intestinal ulceration, and it is explicitly stated in Dr. Welch's note that he is of the opinion that the fat-necroses were not the result of a primary colon infection. It was more probable, in his opinion, that the organisms gaining entrance into the system through the intestinal ulceration reached these areas which already existed. In a number of other instances since then culture-experiments by Prof. Welch have remained entirely without result.

The true cause, then, of these fat-necroses is not entirely settled. No one to-day believes in the original views of Balser with regard to the overgrowth of fatty tissue.

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[1] Festschrift R. Virchow, Berlin, 1891.

[2] Hildebrand recently experimented by tying the pancreatic duct in cats, and in other cases introducing pieces of pancreas into the abdominal cavities of other animals. He asserts that wherever the tissues were exposed to the action of pancreatic juice, alterations resulted which were identical to the fat-necroses observed in man. His experiments led him to believe that these changes are due to the fat-splitting ferment, not to trypsine. La Semaine Médicale, April, 1895, p. 193.

[3] Trans. Path. Soc., London, 1893.

[4] Verhandl. d. xi. Cong. f. Innere Med., Wiesbaden, 1892, p. 451.

[5] Medical News, 1891, v. lix. p. 669.

Rolleston's idea is ingenious, but purely speculative.

It is an undoubted fact, as pointed out by Balser, that fat-necroses may be found in a very considerable number of instances in the interlobular pancreatic fat of individuals who have shown no symptoms pointing to the process during life. These observations have been frequently confirmed in the pathological institute of this university. It is also undoubtedly true that in many of these instances there is no gross evidence of pancreatic disease, while in the great majority of the cases there is nothing to suggest that the condition is purely necrobiotic or marantic. In a like manner it is difficult to account for these necroses by the assumption that they are of infectious origin, particularly in that cultures have so often proved entirely sterile. Especially suggestive is the fact that even in cases associated with marked pancreatitis of undoubted infectious nature cultures have also been sterile. The exact etiological relation of disseminated fat-necrosis to pancreatic disease is not, then, by any means settled. That the process may occur without evidence of pancreatic disease is undoubted. In these instances, however, the areas are almost always limited to the interlobular fat-tissue of the pancreas. On the other hand, it is very probable that the great majority of cases of acute pancreatitis are associated with this process, a proportion probably much larger than indicated by the cases originally collected by Fitz.

The writer has had the good fortune to observe, in the past six years, six cases of acute pancreatitis at autopsy and one at operation. Four of these cases he has been able to follow clinically. In six of these seven instances the process was associated with disseminated fat-necrosis. The only instance in which this association was not present was a case of a small abscess in the pancreas involving an area no larger than a walnut. Here the symptoms produced were not referable to the pancreas, but to complete biliary obstruction caused by implication of the common duct. This case was reported by Dr. Fitz in 1890.[1]

While, as has been said, the relation of disseminated fat-necrosis to acute pancreatitis is not definitely settled, the researches of Langerhans are certainly very suggestive. The process seems in almost all instances to take its origin from the region of the pancreas. The affected areas are usually quite sterile. It has, apparently, been shown that exactly similar changes may be produced by the action of pancreatic juice upon fatty tissue. In the great majority of instances of acute pancreatitis these areas are present. The pancreatic affection would seem in these instances to be certainly infectious in origin, while the individual areas of fat-necrosis are sterile. In view of these facts one can but recognize the possibility that the sequence of events may be, as suggested by

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[1] Trans. Assoc. Amer. Phys., 1890.

Langerhans, a primary lesion of the pancreas which offers the opportunity for the escape of the fat-splitting ferment from the organ into the surrounding tissue, and secondary disseminated fat-necrosis, which is inflammatory only in its remote origin; this, by its extension and progress, may lead to most serious results (sequestration, gangrene of the pancreas, parapancreatic suppuration). In this particular instance it is probable that the primary process, whether in the pancreas or in the fatty tissue, was of some duration, as testified to by the several attacks from which the patient had suffered during the past two years. Clinically the case is of considerable interest in showing the possibility and importance of early diagnosis and operation in certain cases of acute pancreatitis. It is, I believe, the second case reported in literature in which a correct diagnosis of acute pancreatitis has been made—the first in which the diagnosis has been followed by a successful operation. That recovery may occur where the process has been most extensive has been shown by the cases of Trafoyer[1] and Chiari,[2] where large portions of the necrotic pancreas were passed by the rectum. This, however, is an outcome which we can expect in but a small proportion of the cases. The great majority, if not fatal during the first few days, would lead probably to a fatal general peritonitis. It is probable, then, that in a certain number of instances where the process is not acutely fatal, and yet is followed by extensive suppuration or sloughing, timely operation may, as in this case, save the life of the patient.

[Since this article was written two very similar cases have been reported, in each of which an ante-mortem diagnosis was made.

In the first case, reported by Körte (*Semaine Médicale*, April, 1895, p. 193), operation and drainage were followed by temporary relief. The patient died, however, eight days later.

In the second case, reported by Atkinson, an operation was not attempted (*Journ. of the Amer. Med. Assoc.*, 1895, xxiv. p. 999).

Cutler (*Boston Med. and Surg. Journal*, 1895, cxxxii. 354) reports also two cases of acute hemorrhagic pancreatitis, in one of which an ante-mortem diagnosis was made.]

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[1] Wiener med. Woch., 1880, xxx. 139, 164.

[2] Ibid. p. 142